Editorials

Announcing a New Series

IN THIS ISSUE OF THE WESTERN JOURNAL OF MEDICINE, you will find papers that formally launch our medical informatics enterprise. They start on pages 118 and 123.[1,2] We are also delighted to have an editorial by two eminent specialists on this topic.[3] As always, we aim to be of practical value to clinicians who care for and about patients. We want to present reliable, usable information about a field with current utility and great potential. Clarity is our goal. Future topics will include searching the literature more effectively, using handheld computers in clinical medicine, using multimedia to discover patients' preferences, and providing cost-benefit analyses. Russell Altman, MD, PhD, Assistant Professor of Medicine at Stanford University School of Medicine, is taking the lead in the design of this section and the recruiting of its authors. Please submit any suggestions or papers on this topic to his attention (see his article) or send me your suggestions or comments.

LINDA HAWES CLEVER, MD
Editor

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1. Altman RB. Ten grand challenges for medical informatics. West J Med 1997 Feb; 166:118–122
2. Harris ED Jr. Electronic mail: a physician extender? West J Med 1997 Feb; 166:123–125
3. Pauker SG, Stahl JE. Medical informatics: where the action is [editorial]. West J Med 1997 Feb; 166:148–150

Medical Informatics: Where the Action Is

INFORMATION IS the essence of medicine: we create it; we collect it; we search for it; we adapt it; we drown in it; and at times, we ignore it. Although it is central to medicine, the study of biomedical information is a relatively new formal discipline. Lying at the intersection of information theory, cognitive science, artificial intelligence, and medicine, medical informatics extends them all. It focuses on understanding how we use information, hypothesizes how we might use information better, implements those hypotheses as programs and systems, and observes the performance of those theories and tools.

Medical informatics is not simply medical computing, telecommunications, or information engineering, but a dialogue among physicians, patients, and medical informaticians—specialists in medical information. Medical informatics is a science that seeks and develops new knowledge, builds new theories, and organizes principles and solutions based on the results of previous experiments. Because informatics is so central to the practice of medicine and develops tools to solve real problems in everyday clinical practice, investigators in cognitive science and artificial intelligence have often sought this arena for exploring their hypotheses.

Two decades ago we were constrained by the "horsepower" of existing computers and our ability to deliver information and computer cycles to the desktop. Today we are constrained only by our ability to understand how information is now used and how it should be used. Although we are still concerned about drowning in information (from the literature, databases, and our individual patients), the modern tools of desktop information access (browsers, clients, compact disks, the World Wide Web, and evolving desktop "push" technologies) diminish our concern a bit. Medical informatics is the science that helps provide medicine the power and the benefits of the age of information.

A journey to the promised land rarely has been free of challenges. Beginning with this issue, the *Journal* reviews the current status and the research and development agenda of medical informatics. Russell Altman, MD, PhD, lays down a gauntlet in terms of infrastructure, performance, and evaluation.[1] His "ten challenges" focus on the products and processes of clinical informatics. We offer here a different set, one that identifies the challenges to medicine that informatics should help us address.

Teaching Doctors to Program

Central to the practice of medicine should be the ability to break a complex problem into manageable parts, examine those components, formulate solutions in discrete steps, and combine those subroutines into an organized, considered plan. That process of dissection, analysis, and integration forms the core of both computer programming and decision analysis, two of the central disciplines of informatics. As clinicians, we must become more adept at framing and analyzing the clinical problems we confront. As informaticians and teachers, we must share that skill with our students and colleagues.

Dealing With Time

Since the inception of medical informatics perhaps two decades ago, we have been challenged by time: how to represent time and recurrent events in clinical data or structured knowledge, how to deliver the right information when a clinician needs it, or how to interact with clinicians while respecting their most precious commodity, their time. By providing timely and focused feedback to clinicians, informatics can shape changes in behavior and performance. The flip side of this just-in-time information delivery is "on the fly" capture of clinical data. Gathering the information must be no more obtrusive than sticking a carbon paper under the notes clinicians write.

Making Specialists From Generalists

In medicine, this is the era of the generalist in which the emphasis is on continuity, primary care that recognizes the whole patient, and the limitation of perhaps unnecessary costs. Physicians and patients increasingly confront guidelines, algorithms, practice patterns, and care plans, all tools of generalization. But "one size fits all" can too easily become "no size fits anybody." Although medical informatics often addresses the mythical average patient, our technologies can and should support individualization in patient care. An algorithm or guideline far too complex to capture on paper or to recall from memory can be adapted to individual patients and delivered to clinicians' desktops. Rather than undermining clinical skill, intuition, and creativity, medical informatics might be used to customize care and to provide primary care clinicians with the knowledge base of a specialist.

Understanding Information

Data, information, and knowledge come in many forms, ranging from written notes and test results, to narrow databases collected in a clinical trial, to broader databases of fledgling electronic medical records, to the medical literature, meta-analyses, and even algorithms (such as guidelines, logistic regressions, and prediction rules) and computer programs. Medical knowledge begins as a collection of facts that are then organized into theories. The information is then compiled and digested into knowledge. The challenge lies in accessing and learning from these diverse sources and levels of information in the context of the real world, replete with errors, inconsistencies, and noise. Clinicians' strength lies perhaps in their ability to interpret our ambiguous world, form contexts, and frame questions. Computers bring focused computational power, access to information, and perhaps enforced consistency. A collaboration between neural nets based in the silicon of computer chips and those based in the carbon of clinicians can improve clinical care.

Education In Situ: Updating Knowledge

Physicians are effective learners. Although they absorb information like sponges, they seem to incorporate new knowledge better at the bedside or in a "case-based" mode than from lectures or even brilliant review articles. Decades of training have taught physicians to remember, but rarely how to forget. The challenge is replacing old information with new, presumably more correct, knowledge. On the first day of medical school, we were told, "Half the facts you will learn are wrong, but we don't know which half!" Sadly, or perhaps wonderfully, that insight remains true. Informatics can provide the key to the challenge of updating knowledge. The facts we deliver can always be current, and because they can be presented when they are needed, that new information is far more likely to be linked to and update physicians' long-remembered knowledge.

Making Tradeoffs

Decision making lies at the heart of medicine. Medical decisions can be difficult because they must often be made with inadequate information, under uncertainty, and in real time and must reflect tradeoffs between short-term risk and long-term gains, between length and quality of life, and between the individual and society. Decision support remains one of the core tasks of medical informatics. Decision science has increasingly been incorporated in the medical curriculum, but its formal techniques require both experience and a modicum of computational power to be practical. Informatics can deliver both to the bedside.

Understanding Cognition and Supporting the Clinician

Because information management is so central to medical practice, the products of medical informatics will touch us in an intimate way. Although clinicians trained during the information age may develop a different cognitive style than did their teachers, the products of informatics must support clinicians from both eras. Our styles will surely evolve as the information provided and its medium and format change, but the change will be slow and incremental. In the meantime, medical informaticians must take care not to interfere with the performance of experienced practitioners; information must be presented in a form that takes advantage of and amplifies their hard-won skills. Just as some computer programs may monitor clinicians for errors in fact, in deduction, or in overlooking data, clinicians must apply common sense and clinical judgment to the computer's suggestions. Informaticians must support this partnership with clinicians.

Balancing Access With Confidentiality and Data Integrity

The ease and timeliness of access to information and our ability to keep these data secure are innately in conflict. We demand that information be provided just when we need it and collected just as we generate it—a seamless integration into our patterns of practice. But we also demand that information be kept from prying eyes and voracious databases and that it be correct, intact, and valid. These are conflicting goals; any system will be a compromise. When we evaluate a diagnostic test, we understand that sensitivity and specificity can increase only by improving the test itself, not by simply choosing a different operating point. Similarly, informatics can succeed in improving access, security, fidelity, and data integrity only by introducing better technologies.

Industrializing Medicine

Clinical medicine has been a cottage industry that the artisan physician controlled. From time immemorial, physicians have been repositories of information that we shared, carefully and selectively, with our patients. But now our patients arrive, having surfed the Web, with newer and perhaps more complete information than we are able to recall or have had time to collect. Advertisers no longer target only clinicians; print and electronic media inundate patients with new choices and new questions. Just as the industrial revolution transformed western civilization two centuries ago, so will the information revolution transform how physicians practice medicine and how patients receive and participate in their care. Increasingly, clinical practice will become a collaboration between physicians and patients. One of the challenges for informatics will be to provide patients with information of sufficient quality and the knowledge of how to integrate it with the skills of their physicians. Analogously, the information base and skill set provided to clinicians must recognize and complement the new role of patients.

Evaluating Outcomes

Medical informatics develops products that affect clinical practice and will potentially affect the outcomes of clinical care. The evaluation of these new technologies must go beyond examining their premises or exploring the various nooks and crannies of their logic, notwithstanding the complexities of even those limited goals. Clinicians and informaticians (two broadly overlapping sets of professionals) must examine how these programs, systems, and theories change the results of health care. If health outcomes are improved and costs are lowered—not an unreasonable expectation for these new technologies—then arguments about cost-effectiveness become moot. We need be concerned about cost-effectiveness only if costs increase and health outcomes improve. In that case, we might estimate how much we must spend for each unit increase in health and compare that marginal ratio with our willingness to pay for health.

Because medical informatics concerns understanding information and how we interact with it, clinicians and informaticians must communicate if the field is to progress. This series in the *Journal* is an important step. The real challenge facing medical informatics is not in developing new applications, building newer and faster computers, delivering more bits per second to the desktop, or even collecting, organizing, and validating information. Rather, our challenge is to maintain an open dialogue among informaticians, clinicians, and patients. To succeed will require constant effort; to fail will doom us to losing control of our destiny.

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A Fragile Enterprise

The opposite of a correct statement is a false statement. But the opposite of a profound truth may well be another profound truth.

NIELS BOHR

THE BASIC TENETS of heredity have seemed clear for more than 100 years, and until recently, it was thought that the inheritance of most familial disorders could be understood in terms of the principles articulated by Mendel and subsequently refined by others. Genetic diseases should be transmitted in families in patterns consistent with autosomal dominant, autosomal recessive, or X-linked modes of inheritance. In the past few years, however, there has been an explosion of knowledge relating to human conditions that are inherited in nonmendelian ways. These newly described genetic mechanisms include mitochondrial inheritance in which traits may be exclusively matrilineally inherited, genomic imprinting in which genes contributed by a father and mother are not equally expressed in the offspring, and genomic instability in which the immutable transmission of DNA sequence from parent to child turns out to lack the fidelity we had expected. The so-called fragile X syndrome, which is reviewed by Hagerman elsewhere in this issue of the *Journal*,[1] is in the last category.

The fragile X syndrome is the most common inherited cause of mental retardation. The first clear pedigree of a family with this disorder was reported in 1943. The characteristic cytogenetic finding was described in 1969, but it was not until 1991 that the responsible gene *FMR1* (for fragile X mental retardation) was identified and characterized.[2] It should be pointed out that although most cases of X-linked mental retardation with a fragile site visible on karyotype are due to abnormalities of the *FMR1* gene, some families have defects in other genes nearby. The normal protein product of the *FMR1* gene binds to certain RNA molecules, but its function has not been fully defined. It does seem, however, that the loss of function of the *FMR1* protein is responsible for most of the phenotypic features of the fragile X syndrome. For example, when a small mutation destroys the ability of the *FMR1* protein to bind to RNA, or when *FMR1* gene function is disrupted in mice, most of the features of the disorder are present. In the vast majority of human patients with the fragile X syndrome, however, the mechanism that leads to the loss of function of *FMR1* is different. The *FMR1* gene is one of a growing family of genes found to contain within its structure a repeating series of nucleotides. In this case, the sequence is $(CGG)_n$. The repeat is located within the so-called 5′ untranslated portion of the gene, which is transcribed from DNA into messenger RNA, but does not actually encode any amino acids in the final protein product. In normal persons, the number of CGG repeats in the *FMR1* gene ranges between 6 and 52. In patients with the full-blown fragile X syndrome, the number of repeats is greater than 230 and may be more than 1,000. In ways that are not yet fully understood, the expanded repeats shut off expression of the gene (associated with the methylation of nearby controlling DNA sequences) and lead to an altered chromatin structure of that region of the X chromosome. This results in the cytogenetic appearance of a fragile site.

Recognition of the expansion of a trinucleotide repeat in this gene in patients with the fragile X syndrome not only opens the door to understanding the mechanism of control of *FMR1* expression, but also provides insight into the processes by which alterations in the number of repeats may arise from one generation to the next. For some time, we have known of clinically normal men who have